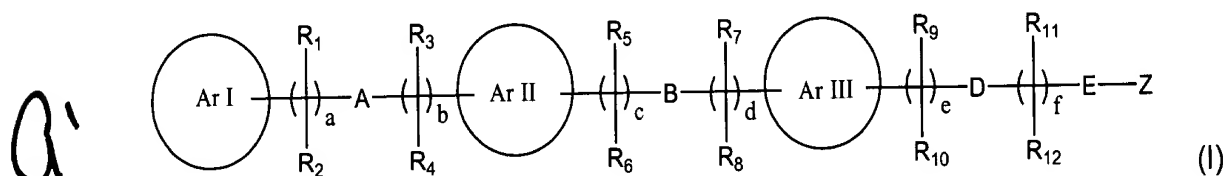
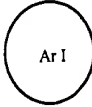




1. (Twice Amended) A compound of formula I

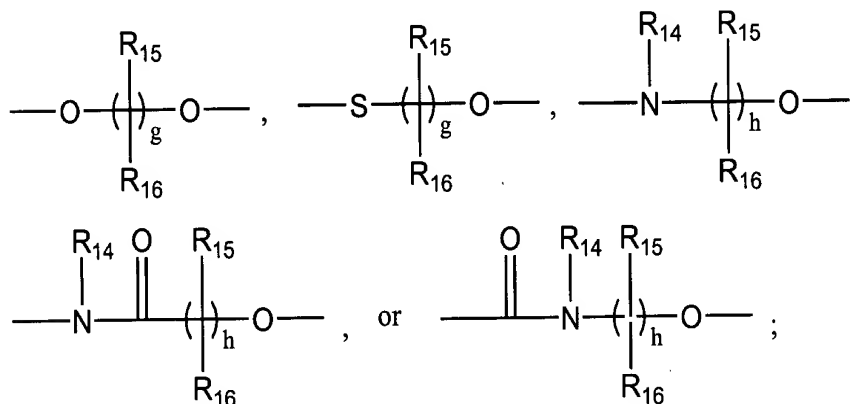


wherein:

 is heteroaryl, which is optionally substituted by one or more ring system substituents;

 and  are, independently, aryl, which are optionally substituted by one or more ring system substituents;

A is -O-, -S-, -SO-, -SO<sub>2</sub>-, -NR<sub>13</sub>-, -C(O)-, -N(R<sub>14</sub>)C(O)-, -C(O)N(R<sub>15</sub>)-,  
-N(R<sub>14</sub>)C(O)N(R<sub>15</sub>)-, -C(R<sub>14</sub>)=N-, a chemical bond,



B is -O-, -S-, -SO-, -SO<sub>2</sub>-, -NR<sub>17</sub>-, ethynylene, -C(O)-, -N(R<sub>18</sub>)C(O)-, or -C(O)NR<sub>18</sub>-;

D is -O-, -S-, -NR<sub>19</sub>-, a chemical bond, ethynylene, -N(R<sub>20</sub>)C(O)-, -C(O)-, or  
-C(O)N(R<sub>20</sub>)-;

E is a chemical bond or an ethylene group;

a is 0-4;

b is 0-4;

a'

c is 0-4;

d is 0-5;

e is 0-4;

f is 0-6;

g is 1-4;

h is 1-4;

R<sub>1</sub>, R<sub>3</sub>, R<sub>5</sub>, R<sub>7</sub>, R<sub>9</sub>, and R<sub>11</sub>, are independently hydrogen, halogen, alkyl, carboxyl, alkoxy carbonyl or aralkyl;

R<sub>2</sub>, R<sub>4</sub>, R<sub>6</sub>, R<sub>8</sub>, R<sub>10</sub> and R<sub>12</sub>, are independently -(CH<sub>2</sub>)<sub>q</sub>-X;

q is 0-3;

X is hydrogen, halogen, alkyl, alkenyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroaralkyl, hydroxy, alkoxy, aralkoxy, heteroaralkoxy, carboxyl, alkoxy carbonyl,

tetrazolyl, acyl, acylHNSO<sub>2</sub>-, -SR<sub>23</sub>, Y<sup>1</sup>Y<sup>2</sup>N- or Y<sup>3</sup>Y<sup>4</sup>NCO-;

Y<sup>1</sup> and Y<sup>2</sup> are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl, or one of Y<sup>1</sup>

and Y<sup>2</sup> is hydrogen or alkyl and the other of Y<sup>1</sup> and Y<sup>2</sup> is acyl or aroyl;

Y<sup>3</sup> and Y<sup>4</sup> are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl;

Z is R<sub>21</sub>O<sub>2</sub>C-, R<sub>21</sub>OC-, cyclo-imide, -CN, R<sub>21</sub>O<sub>2</sub>SHNCO-, R<sub>21</sub>O<sub>2</sub>SHN-, (R<sub>21</sub>)<sub>2</sub>NCO-, R<sub>21</sub>O-2,4-thiazolidinedionyl, or tetrazolyl; and

R<sub>21</sub> is hydrogen, alkyl, aryl, cycloalkyl, or aralkyl;

R<sub>13</sub>, R<sub>17</sub>, R<sub>19</sub> and R<sub>23</sub> are independently R<sub>22</sub>OC-, R<sub>22</sub>NHOC-, hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, heteroaralkyl, or aralkyl;

R<sub>14</sub>, R<sub>15</sub>, R<sub>16</sub>, R<sub>18</sub> and R<sub>20</sub> are independently hydrogen, alkyl, aralkyl, carbonyl, or alkoxy carbonyl;

or R<sub>14</sub>, and R<sub>15</sub> taken together with the carbon and nitrogen atoms through which they are linked form a 5 or 6-membered azaheterocyclyl group; or

when a is 2-4, then vicinal R<sub>1</sub> radicals taken together with the carbon atoms to which the R<sub>1</sub> radicals are linked form an ethylene group; or

when b is 2-4, then vicinal R<sub>3</sub> radicals taken together with the carbon atoms to which the R<sub>3</sub> radicals are linked form an ethylene group; or

when c is 2-4, then vicinal R<sub>5</sub> radicals taken together with the carbon atoms to which the R<sub>5</sub> radicals are linked form an ethylene group; or

when d is 2-5, then vicinal R<sub>7</sub> radicals taken together with the carbon atoms to which the R<sub>7</sub> radicals are linked form an ethylene group; or

a' when e is 2-4, then vicinal R<sub>9</sub> radicals taken together with the carbon atoms to which the R<sub>9</sub> radicals are linked form an ethylene group; or

when f is 2-6, then vicinal R<sub>11</sub> radicals taken together with the carbon atoms to which the R<sub>11</sub> radicals are linked form an ethylene group; and

R<sub>22</sub> is hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, heteroaralkyl, or aralkyl; or

a pharmaceutically acceptable salt thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof;

wherein

"alkyl" is an aliphatic hydrocarbon group which is straight or branched having 1 to about 20 carbon atoms and is optionally substituted by one or more alkyl group substituents;

"aryl" is an aromatic monocyclic or multicyclic ring system of about 6 to about 14 carbon atoms, which is optionally substituted by one or more ring system substituents;

"heteroaryl" is an aromatic monocyclic or multicyclic ring system of about 5 to about 14 carbon atoms, in which at least one of the carbon atoms in the ring system is replaced by nitrogen, oxygen or sulfur, which is optionally substituted by one or more ring system substituents;

"heterocyclyl" is a non-aromatic saturated monocyclic or multicyclic ring system of 3 to about 10 carbon atoms, in which at least one of the carbon atoms in the ring system is replaced by nitrogen, oxygen or sulfur, which is optionally substituted by one or more ring system substituents;

"heteroaralkyl" is a heteroaryl-alkyl group, wherein the heteroaryl and alkyl groups are as defined above;

an "alkyl group substituent" is halo, carboxy, cycloalkyl, cycloalkenyl, heterocyclyl, heterocyclenyl, aryl, alkoxy, alkoxycarbonyl, aralkoxycarbonyl,

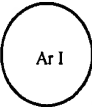
heteroaralkoxycarbonyl, or  $Y^1Y^2NCO-$ , wherein  $Y^1$  and  $Y^2$  are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl, or  $Y^1$  and  $Y^2$  taken together with the nitrogen atom to which  $Y^1$  and  $Y^2$  are attached form heterocyclyl

a'

wherein the substituents may contain further alkyl group substituents or ring system substituents as recited herein; and

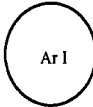
a "ring system substituent" is alkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroaralkyl, hydroxy, alkoxy, aryloxy, aralkoxy, acyl, aroyl, halo, nitro, cyano, carboxy, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, alkylsulfonyl, arylsulfonyl, heteroarylsulfonyl, alkylsulfinyl, arylsulfinyl, heteroarylsulfinyl, alkylthio, arylthio, heteroarylthio, aralkylthio, heteroaralkylthio, fused cycloalkyl, fused cycloalkenyl, fused heterocyclyl, fused heterocyclenyl, arylazo, heteroarylazo,  $R^aR^bN-$ ,  $R^cR^dNCO-$ ,  $R^cO_2CN-$ , or  $R^cR^dNSO_2-$  wherein  $R^a$  and  $R^b$  are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl, or one of  $R^a$  and  $R^b$  is hydrogen or alkyl and the other of  $R^a$  and  $R^b$  is aroyl or heteroaroyl, and  $R^c$  and  $R^d$  are independently hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, cycloalkenyl, heterocyclyl, heterocyclenyl, aralkyl or heteroaralkyl and, where the ring is cycloalkyl, cycloalkenyl, heterocyclyl or heterocyclenyl, the ring system substituent may also include methylene, oxo and thioxo on carbon atoms thereof,

wherein the substituents may contain further alkyl group substituents or ring system substituents as recited herein.

2. (Amended) A compound according to claim 1 wherein  is optionally substituted azaheteroaryl.

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Q<sup>2</sup>

20. (Twice Amended) A compound according to claim 1 wherein  is an optionally substituted quinolinyl, quinoxalinyl, quinazolinyl, isoquinolinyl, benzoxazolyl, benzimidazolyl, benzothiazolyl, benzofuranyl, benzothiophenyl, oxazolyl, thiazolyl,

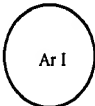
oxadiazolyl, isoxazolyl, imidazolyl, pyrazol-yl, thiadiazolyl, triazolyl, pyridyl, pyrimidinyl, pyrazinyl, or pyridazinyl group.

a<sup>2</sup>



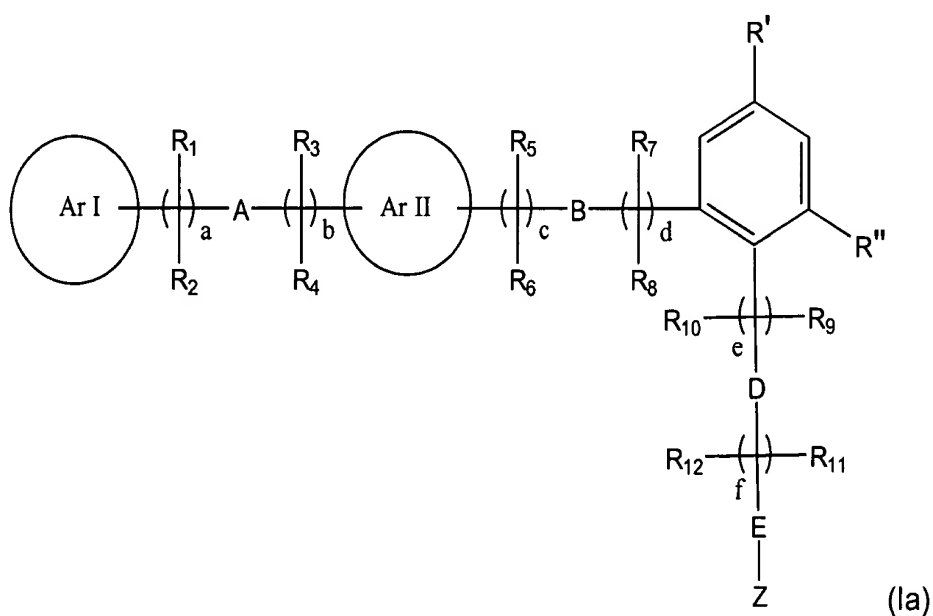
21. (Amended) A compound according to claim 1 wherein is unsubstituted quinolin-2-yl, 3-substituted quinolin-2-yl, 4-substituted quinolin-2-yl, 6-substituted quinolin-2-yl or 7 substituted quinolin-2-yl; an unsubstituted quinoxalin-2-yl, 3-substituted quinoxalin-2-yl, 6-substituted quinoxalin-2-yl or 3,6-disubstituted quinoxalin-2-yl; unsubstituted quinazolin-2-yl, 4-substituted quinazolin-2-yl or 6-substituted quinazolin-2-yl; unsubstituted isoquinolin-3-yl, 6-substituted isoquinolin-3-yl or 7-substituted isoquinolin-3-yl; 2-substituted-oxazol-4-yl or 2,5 disubstituted-oxazol-4-yl; 4-substituted oxazol-2-yl or 4,5-disubstituted-oxazol-2-yl; 2-substituted thiazol-4-yl or 2,5-disubstituted thiazol-4-yl; 4-substituted thiazol-2-yl or 4,5-disubstituted-thiazol-2-yl; 5-substituted-[1,2,4]oxadiazol-3-yl; 3-substituted-[1,2,4] oxadiazol-5-yl; 5-substituted-imidazol-2-yl or 3,5-disubstituted-imidazol-2-yl; 2-substituted-imidazol-5-yl or 2,3-disubstituted-imidazol-5-yl; 3-substituted-isoxazol-5-yl; 5-substituted-isoxazol-3-yl; 5-substituted-[1,2,4] thiadiazol-3-yl; 3-substituted-[1,2,4]-thiadiazol-5-yl; 2-substituted-[1,3,4]-thiadiazol-5-yl; 2-substituted-[1,3,4]-oxadiazol-5-yl; 1-substituted-pyrazol-3-yl; 3-substituted-pyrazol-5-yl; 3-substituted-[1,2,4]-triazol-5-yl; 1-substituted-[1,2,4]-triazol-3-yl; 3-substituted pyridin-2-yl, 5-substituted pyridin-2-yl, 6-substituted pyridin-2-yl or 3,5-disubstituted pyridin-2-yl; 3-substituted pyrazin-2-yl, 5-substituted pyrazin-2-yl, 6-substituted pyrazin-2-yl or 3,5 disubstituted-pyrazin-2-yl; 5-substituted pyrimidin-2-yl or 6-substituted-pyrimidin-2-yl; 6-substituted-pyridazin-3-yl or 4,6-disubstituted-pyridazin-3-yl; unsubstituted -benzothiazol-2-yl or 5-substituted-benzothiazol-2-yl; unsubstituted benzoxazol-2yl or 5-substituted-benzoxazol-2yl; unsubstituted -benzimidazol-2-yl or 5-substituted-benzimidazol-2-yl; unsubstituted -thiophen-2yl, 3-substituted -thiophen-2yl, 6-substituted -thiophen-2yl or 3,6-disubstituted-thiophen-2yl; unsubstituted -benzofuran-2-y, 3-substituted-benzofuran-2-yl, 6-substituted-benzofuran-2-yl or 3,6-disubstituted-benzofuran-2-yl; 3-substituted-benzofuran-6-yl or 3,7-disubstituted-benzofuran-6-yl.

A<sup>2</sup>

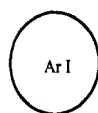
22. (Amended) A compound according to claim 21 wherein  is substituted by a substituent selected from the group consisting of phenyl, substituted-phenyl, thienyl, substituted thienyl, cycloalkyl, straight or branched lower alkyl, fluoro, chloro, alkoxy, aralkyloxy, trifluoromethyl and trifluoromethyloxy.

A<sup>3</sup>

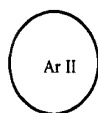
27. (Twice Amended) A compound of formula (Ia)



wherein:

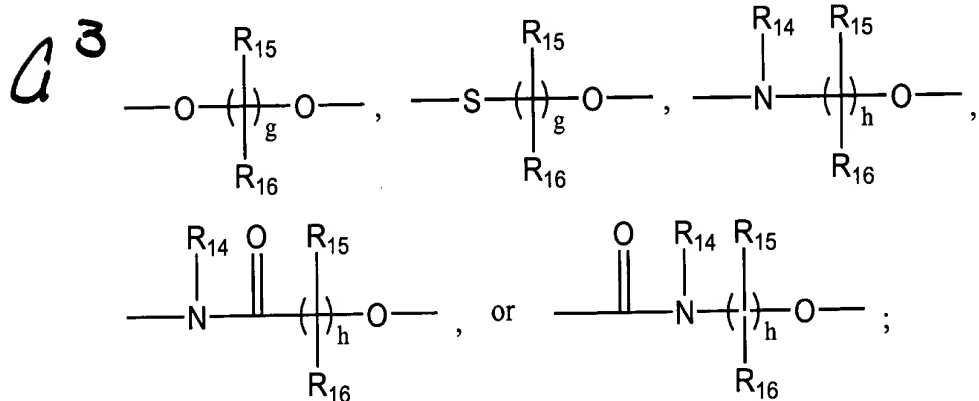


is heteroaryl, which is optionally substituted by one or more ring system substituents;



is aryl, which is optionally substituted by one or more ring system substituents;

A is -O-, -S-, -SO-, -SO<sub>2</sub>-, -NR<sub>13</sub>-, -C(O)-, -N(R<sub>14</sub>)C(O)-, -C(O)N(R<sub>15</sub>)-,  
-N(R<sub>14</sub>)C(O)N(R<sub>15</sub>)-, -C(R<sub>14</sub>)=N-, a chemical bond,



B is -O-, -S-, -SO-, -SO<sub>2</sub>-, -NR<sub>17</sub>-, ethynylene, -C(O)-, -N(R<sub>18</sub>)C(O)-, or -C(O)NR<sub>18</sub>-;

D is -O-, -S-, -NR<sub>19</sub>-, a chemical bond, ethynylene, -N(R<sub>20</sub>)C(O)-, -C(O)-, or  
-C(O)N(R<sub>20</sub>)-

E is a chemical bond or an ethylene group;

a is 0-4;

b is 0-4;

c is 0-4;

d is 0-5;

e is 0-4;

f is 0-6;

g is 1-4;

h is 1-4;

R<sub>1</sub>, R<sub>3</sub>, R<sub>5</sub>, R<sub>7</sub>, R<sub>9</sub>, and R<sub>11</sub>, are independently hydrogen, halogen, alkyl, carboxyl,  
alkoxycarbonyl or aralkyl;

R<sub>2</sub>, R<sub>4</sub>, R<sub>6</sub>, R<sub>8</sub>, R<sub>10</sub> and R<sub>12</sub>, are independently -(CH<sub>2</sub>)<sub>q</sub>-X;

q is 0-3;

X is hydrogen, halogen, alkyl, alkenyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl,  
heteroaralkyl, hydroxy, alkoxy, aralkoxy, heteroaralkoxy, carboxyl, alkoxycarbonyl,  
tetrazolyl, acyl, acylHNSO<sub>2</sub>-, -SR<sub>23</sub>, Y<sup>1</sup>Y<sup>2</sup>N- or Y<sup>3</sup>Y<sup>4</sup>NCO-;

$Y^1$  and  $Y^2$  are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl, or one of  $Y^1$  and  $Y^2$  is hydrogen or alkyl and the other of  $Y^1$  and  $Y^2$  is acyl or aroyl;

$Y^3$  and  $Y^4$  are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl;

Z is  $R_{21}O_2C-$ ,  $R_{21}OC-$ , cyclo-imide,  $-CN$ ,  $R_{21}O_2SHNCO-$ ,  $R_{21}O_2SHN-$ ,  $(R_{21})_2NCO-$ ,  $R_{21}O-$  2,4-thiazolidinedionyl, or tetrazolyl;

$R'$  and  $R''$  are, independently, hydrogen or ring system substituents;

$R_{21}$  is hydrogen, alkyl, aryl, cycloalkyl, or aralkyl;

$R_{13}$ ,  $R_{17}$ ,  $R_{19}$  and  $R_{23}$  are independently  $R_{22}OC-$ ,  $R_{22}NHOC-$ , hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, heteroaralkyl, or aralkyl;

$R_{14}$ ,  $R_{15}$ ,  $R_{16}$ ,  $R_{18}$  and  $R_{20}$  are independently hydrogen, alkyl, aralkyl, carbonyl, or alkoxy carbonyl;

or  $R_{14}$ , and  $R_{15}$  taken together with the carbon and nitrogen atoms through which they are linked form a 5 or 6-membered azaheterocyclyl group; or

when a is 2-4, then vicinal  $R_1$  radicals taken together with the carbon atoms to which the  $R_1$  radicals are linked form an ethylene group; or

when b is 2-4, then vicinal  $R_3$  radicals taken together with the carbon atoms to which the  $R_3$  radicals are linked form an ethylene group; or

when c is 2-4, then vicinal  $R_5$  radicals taken together with the carbon atoms to which the  $R_5$  radicals are linked form an ethylene group; or

when d is 2-5, then vicinal  $R_7$  radicals taken together with the carbon atoms to which the  $R_7$  radicals are linked form an ethylene group; or

when e is 2-4, then vicinal  $R_9$  radicals taken together with the carbon atoms to which the  $R_9$  radicals are linked form an ethylene group; or

when f is 2-6, then vicinal  $R_{11}$  radicals taken together with the carbon atoms to which the  $R_{11}$  radicals are linked form an ethylene group; and

$R_{22}$  is hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, heteroaralkyl, or aralkyl;

or

a pharmaceutically acceptable salt thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.



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36. (Amended) A compound according to claim 27 wherein:

a = 1;

A is -O-;

b = 0;

c = 0;

B is -O-;

d = 1;

e = 0;

f = 0;

D and E are a chemical bond;

R' is hydrogen;

R'' is methyl;

Z is -CO<sub>2</sub>H.

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51. (Amended) A method according to claim 50 wherein the physiological disorder is associated with a physiological detrimental blood level of insulin, glucose, free fatty acids (FFA), or triglycerides.

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58. (Amended) The method according to claim 51, wherein the physiological disorder is a cardiovascular condition.

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68. (Amended) A method according to claim 67 wherein the physiological disorder is associated with a physiological detrimental blood level of insulin, glucose, free fatty acids (FFA), or triglycerides.

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75. (Amended) The method according to claim 67, wherein the physiological disorder is a cardiovascular disorder.

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89. (Amended) A compound as claimed in claim 20, wherein the ring system substituent is selected from the group consisting of phenyl, substituted-phenyl, thienyl, substituted thienyl, cycloalkyl, straight or branched lower alkyl, fluoro, chloro, alkoxy, aralkyloxy, trifluoromethyl and trifluoromethoxy.

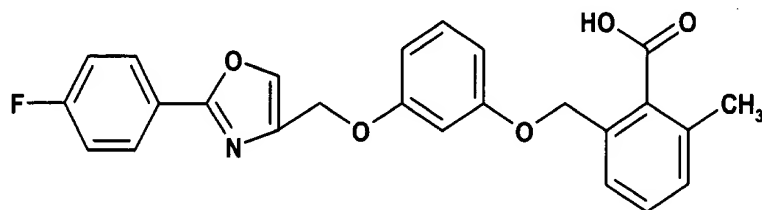
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a<sup>10</sup>

91. (Amended) A compound as claimed in claim 31, wherein R<sup>n</sup> is methyl.

94. (Amended) A compound as claimed in claim 1, wherein the compound is

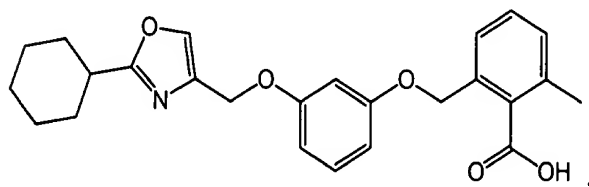
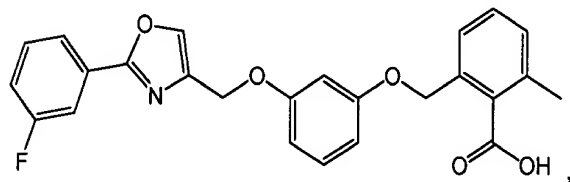
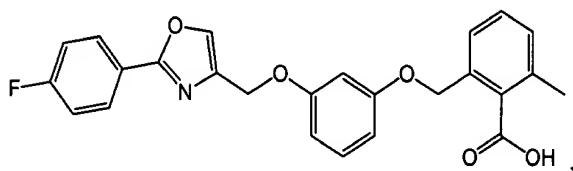
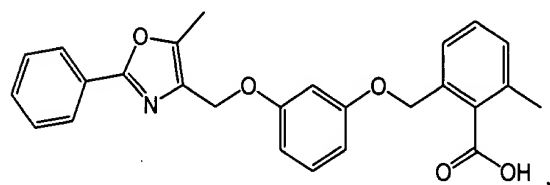
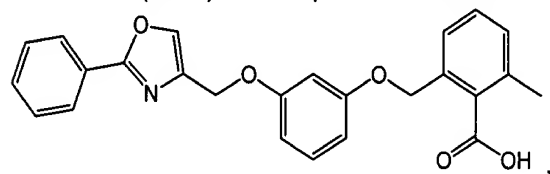
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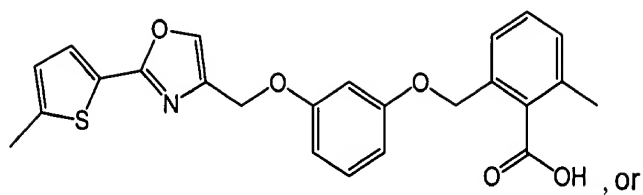


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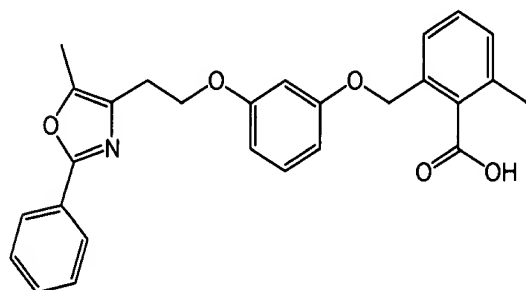
or a pharmaceutically acceptable salt, hydrate or solvate thereof.

95. (New) A compound as claimed in claim 1, wherein the compound is



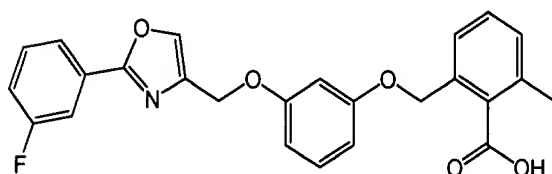
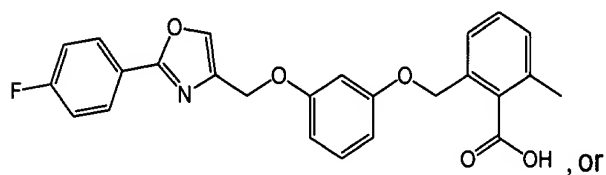
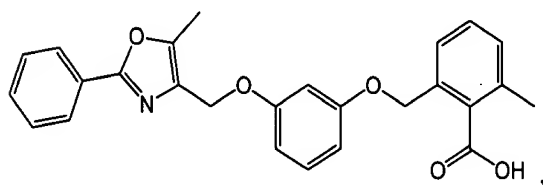
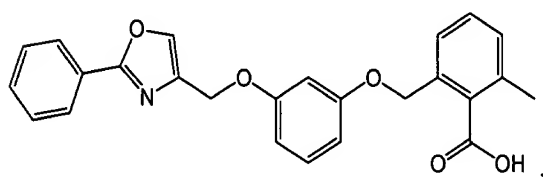


a<sup>11</sup>



or a pharmaceutically acceptable salt, hydrate or solvate thereof.

96. (New) A compound as claimed in claim 1, wherein the compound is



or a pharmaceutically acceptable salt, hydrate or solvate thereof.